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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/578,507	05/26/00	RAMASUBRAMANYAN	N 2827-4
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EXAMINER

SANDALS, W

ART UNIT

PAPER NUMBER

1636

DATE MAILED: 10/01/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/578,507

Applicant(s)

Ramasubramanyan

Examiner

William Sandals

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on May 26, 2000
- 2a) ☐ This action is FINAL.
- 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-53 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-53 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5 & 6
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

DETAILED ACTION

Drawings

1. The drawings as submitted on May 26, 2000, have been approved by the draftsman.

Specification

2. The use of the trademarks SEPHAROSE, STREAMLINE, SYBER GOLD, POLY-FLO, DNA ETOX, KINETIC-QCL and Q HYPER D have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

3. Claim 14 is objected to because of the following informalities: Claim 14 recites "claims 12", where "claims" is plural and should be singular. Appropriate correction is required.
4. Claim 17 is objected to because of the following informalities: Claim 17 recites "a first conditions", "a second conditions" and "a third conditions", where "conditions" is plural and should be singular. Appropriate correction is required.

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5. Claim 17 at line 12 recites “remove relaxed plasmid DNA from bound first mixture”. A “the” should be inserted between “from” and “bound” .
6. Claim 17 recites at line 15 “said bound second mixture”. The phrase should be rewritten as “said second bound mixture” to be consistent.
7. Claims 27, 28 and 29 are objected to because of the following informalities: Claim 27 recites “a first conditions”, claim 28 recites “a second conditions” and claim 29 recites “a third conditions”, where “conditions” is plural and should be singular. Appropriate correction is required.
8. Claim 41 is objected to because of the following informalities: Claim 41 recites “a first conditions”, “a second conditions” and “a third conditions”, where “conditions” is plural and should be singular. Appropriate correction is required.
9. Claims 47, 48 and 49 are objected to because of the following informalities: Claim 47 recites “a first conditions”, claim 48 recites “a second conditions” and claim 49 recites “a third conditions”, where “conditions” is plural and should be singular. Appropriate correction is required.
10. Claim 48 recites at line 2 “said first bound mixture”. The phrase should be rewritten as “said bound first mixture” to be consistent.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1-29 and 41-53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
13. Claim 1, section "(c)" states "collecting unbound plasmid DNA from said complex and hydrophobic interaction media". The "hydrophobic interaction media" is part of the complex in section "(c)". Therefore, it is not understood how the "hydrophobic interaction media" can be a separate element in this section of the claim. As a result the claim is vague and indefinite.
14. Claim 1, line 12 states "the method is conducted in the absence of solvents". Since water is a solvent, and water is required for the performance of the method, this limitation has no clear meaning, and is inconsistent with the teachings of the specification. For the purposes of examination, it has been assumed that the intent of the claim is to be performed without non-polar solvents.
15. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by

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raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 6 and 9 recite the broad recitation "about 2M", and the base claims 5 and 7 upon which claims 6 and 9 depend recite the narrow limitation of concentration range of "2M to 4M" which is the narrower statement of the range/limitation. "About 2M" carries a limitation which lies outside of the range of "2M", which is the lower limit of the range of the base claims .

16. Claim 15 recites the limitation "or a cross linked agarose backbone" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim. The base claim 14 recites only a "methacrylate polymer or copolymer backbone". Agarose is not a methacrylate polymer or copolymer.

17. Claim 16 recites the limitation "the resin" in line 1. There is insufficient antecedent basis for this limitation in the claim.

18. Claim 44 recites the limitation "or a cross linked agarose backbone" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim. The base claim 14 recites only a "methacrylate polymer or copolymer backbone". Agarose is not a methacrylate polymer or copolymer.

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19. Claim 46 recites the limitation "said resin" in line 1. There is insufficient antecedent basis for this limitation in the claim.
20. Claim 47 recites the limitation "said mixture" in line 2. There is insufficient antecedent basis for this limitation in the claim.
21. Claim 52 recites the limitation "the amount" in line 1. There is insufficient antecedent basis for this limitation in the claim.
22. Claim 52 recites the limitation "media containing" in line 7. There is insufficient antecedent basis for this limitation in the claim.
23. Claim 53 recites the limitation "the mixture" in line 3. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

24. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

25. Claims 17, 18, 20-23, 25, 26, 41-45, 51 and 52 are rejected under 35 U.S.C. 102(b) as being anticipated by either Kapp et al. or Colote et al.

Each of Kapp et al. (see especially the abstract, the figures and materials and methods) or Colote et al. (see especially the abstract, figures, part IV, and materials and methods) taught a

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method of separating and isolating supercoiled plasmid DNA from relaxed plasmid DNA and other host cell impurities by reversed phase chromatography, with a hydrophobic interaction media with C3-C20 pendant groups.

26. Claims 17-23, 25, 30, 31, 34-37, 41-45 and 51-53 are rejected under 35 U.S.C. 102(e) as being anticipated by US 6,214,586.

US 6,214,586 (see especially the summary and column 4) taught a method of separating and isolating supercoiled plasmid DNA from relaxed plasmid DNA and other host cell impurities which are RNA, cellular DNA and endotoxin, by reversed phase chromatography, with a hydrophobic interaction media with C3-C20 pendant groups.

27. Claim 53 is rejected under 35 U.S.C. 102(e) as being anticipated by US 6,197,553.

US 6,197,553 (see especially columns 4-6 and example 4) taught a method of separating and isolating plasmid DNA from endotoxin, by reversed phase chromatography, with a hydrophobic interaction media by using ionic buffer conditions which allow the separation of DNA from endotoxin.

Claim Rejections - 35 USC § 103

28. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

29. Claims 1-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,197,553 in view of Maitra et al., Colote et al., Kapp et al., Ishida et al., US 6,265,168 and US 6,214,586.

The claims are drawn to a method of separating and isolating supercoiled plasmid DNA from relaxed plasmid DNA and other host cell impurities which are RNA, cellular DNA and endotoxin, by elution with reverse phase chromatography at various salt concentrations, with a hydrophobic interaction media with C3-C10 pendant groups, and in the absence of non-polar solvents, detergents, glycols, hexamine cobalt, spermidine and polyvinylpyrrolidone.

US 6,197,553 taught the invention as described in the rejection under 35 USC 102 above.

US 6,197,553 did not teach that the elution was done without non-polar solvents or detergents, nor the various salt concentrations in the elution buffer.

Maitra et al. taught a method of binding of endotoxin to various reverse phase chromatography media (hydrophobic interaction media) and the use of high salt buffers to bind and elute the endotoxin.

Kapp et al. and Colote et al. taught the binding, elution and separation of plasmid DNA's with reverse phase chromatography media (hydrophobic interaction media).

US 6,214,586 taught a method of separating and isolating supercoiled plasmid DNA from relaxed plasmid DNA and other host cell impurities which are RNA, cellular DNA and

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endotoxin, by reversed phase chromatography, which is a hydrophobic interaction media with C3-C20 pendant groups.

US 6,265,168 taught (see especially columns 25-26) the well known use of resin beads and various forms of solid support "backbone" with pendant groups of C3 to C20, and anions and cations which are commonly used in reverse phase chromatography.

Ishida et al. (see the abstract and figures) taught the elution of endotoxin from a reverse phase chromatography media with a buffer concentration in the range of 0-2.5M ammonium sulfate in the absence of non-polar solvents.

It would have been obvious to one of ordinary skill in the art at the time of filing the instant application to combine the teachings of US 6,197,553 with Maitra et al., Colote et al., Kapp et al., Ishida et al., US 6,265,168 and US 6,214,586 because each of US 6,197,553, Maitra et al., Colote et al., Kapp et al., Ishida et al., US 6,265,168 and US 6,214,586 taught the well known and obvious methods of isolation and separation techniques employing reverse phase chromatography hydrophobic interaction media. The above references taught the practice of the instant claimed methods of separation and isolation of plasmid supercoiled DNA, relaxed plasmid or endotoxin.

One of ordinary skill in the art would have been motivated to combine the teachings of US 6,197,553 with Maitra et al., Colote et al., Kapp et al., Ishida et al., US 6,265,168 and US 6,214,586 because reverse phase chromatography (hydrophobic interaction media) is a method which involves the non-polar binding of molecules to the hydrophobic interaction media, and the

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elution of the molecules by increasing the non-polarity of the elution buffer, such that the bound molecules are eluted according to the concentration of non-polar buffer. A buffer such as the ammonium sulphate used in the examples of the instant specification and claims has a higher non-polarity at lower concentrations. This is consistent with the principles of reverse phase chromatography, and is obvious to one of ordinary skill in the art based on the well known principles of reverse phase chromatography which are exemplified in the above references. Kapp et al., Colote et al. and US 6,197,553 each taught the isolation and separation of supercoiled plasmid DNA from relaxed plasmid DNA using well known and obvious methods of reverse phase chromatography with hydrophobic interaction media. US 6,197,533 taught the isolation of supercoiled plasmid DNA from relaxed plasmid DNA and endotoxin using well known and obvious methods of reverse phase chromatography with hydrophobic interaction media. US 6,214,586 taught the isolation of plasmid DNA from endotoxin and RNA using well known and obvious methods of reverse phase chromatography with hydrophobic interaction media. Ishida et al. and US 6,214,586 taught the isolation of endotoxin using well known and obvious methods of reverse phase chromatography with hydrophobic interaction media. Therefore, the teachings of the above references taught the obvious application of well known principles using well known reverse phase chromatography hydrophobic interaction media to isolate, separate and purify supercoiled plasmid from relaxed plasmid which was also separated from host cell contaminants such as endotoxin and RNA. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the

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teachings of US 6,197,553 with Maitra et al., Colote et al., Kapp et al., Ishida et al., US 6,265,168 and US 6,214,586.

With regard to the size of the chromatography beads, beads of this size range are well known to those of ordinary skill in the art and would have been obvious to one of ordinary skill in the art to use for the purpose recited in claims 16, 24, 38 and 46.

Conclusion

30. Certain papers related to this application are *welcomed* to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Friday from 8:30 AM to 5:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Schwartzman can be reached at (703) 308-7307.

Any inquiry of a general nature or relating to the status of this application should be directed to the Zeta Adams, whose telephone number is (703) 305-3291.

William Sandals, Ph.D.

Examiner

September 21, 2001


TERRY MCKELVEY
PRIMARY EXAMINER